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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/665,519	09/22/2003	Andre Stamm	31672-224619	5826

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EXAMINER	
SHEIKH, HUMERA N	
ART UNIT	PAPER NUMBER
1618	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/665,519	STAMM ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-84* is/are pending in the application.

4a) Of the above claim(s) *1-15,56-80,83 and 84* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-55,81 and 82* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Request for Continued Examination under 37 C.F.R. §1.114 and request for extension of time (5 months-granted), both filed 06/23/08 and Applicant's Arguments/Remarks filed 10/26/07 is acknowledged.

Claims 1-84 are pending in this action. Claims 16-55, 81 & 82 are being examined herein. Claims 1-15, 56-80, 83 & 84 have previously been withdrawn (due to non-elected subject matter). No amendments to the claims have been made herein. Claims 16-55, 81 & 82 remain rejected.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 23 June 2008 has been entered.

* * * * *

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 16-25, 32-34, 36-45, 52-54, 81 and 82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boyer (US Pat. No. 4,800,079).

Boyer ('079) teaches a fenofibrate composition comprising granules, wherein each granule comprises an inert core constituted with hydrosoluble carrier particles (lactose, sucrose, glucose), a hydrophilic polymer (polyvinylpyrrolidone) and a fenofibrate layer and a protective layer wherein the fenofibrate is in the form of crystalline microparticles having a particle size of not greater than 30 microns and preferably less than 10 microns (see abstract and reference columns 2-4). Starch (disintegrant) can also be included in the composition (Claims 3 & 7).

Boyer teaches fenofibrate granules wherein the inert matrix is composed by a binder selected from the group comprising: *methacrylic polymers, polyvinylpyrrolidone, mixtures thereof; cellulose derivatives; and polyethylene glycols* (claim 2). The inert core is constituted by a substance selected from the group comprising: *glucose, sucrose, lactose and their equivalents, starch and mixtures thereof* (claim 3). The fenofibrate composition includes a

protective coating layer, representing about 1% by weight of each granule and is formed of a substance selected from the group comprising: *methacrylic polymers, polyvinylpyrrolidone, mixtures thereof; cellulose derivatives; and polyethylene glycols* (claim 4). The amount of binder is such that the quantity of fenofibrate liberated in one hour in an aqueous liquid is not less than 65% (claim 5). The dimensions of the microparticles are *less than 10 microns* (claim 6).

Boyer teaches that the granules obtained are put into capsules with a dose of 250 mg of fenofibrate per capsule. Boyer teaches that the fenofibrate layer is similar to that of a sponge, with the pores containing microparticles of fenofibrate. A binder, methacrylate or polyvinylpyyrolidone, which is soluble in aqueous medium, constitutes the sponge. Once the binder has dissolved, the microparticles of fenofibrate are released. The amount of binder is determined so that at least 65% of the fenofibrate is released in one hour in a water-based liquid medium (col. 3, lines 10-45).

Boyer teaches that the inert grains for forming the inert cores can have a diameter adjusted from 0.3 mm (or 300 microns) to 0.6 mm (or 600 microns) (col. 2, lines 38-51).

In the Example at col. 3, fenofibrate is provided in amounts of 400 kg, inert grains (sugar and/or starch) are provided in amounts of 110 kg and polyvinylpyrrolidone and/or methacrylate are provided in amounts of 20 kg. Thus, the weight ratio of fenofibrate: polyvinylpyrrolidone and/or methacrylate is 20:1.

While Boyer does not explicitly teach the instantly claimed weight ratio of fenofibrate to hydrophilic polymer, nor the instant amounts of fenofibrate, carrier and hydrophilic polymer as claimed in claims 32-33 & 52-53, the Examiner points out that generally, differences in

concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller,* 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). In this instance, Applicants have not demonstrated any superior or unexpected results, which accrue from the claimed weight ratios or amounts. The prior art recognizes and teaches similar formulations comprising similar ingredients, intended to treat the same problems as that desired by Applicants. No patentable distinction has been observed, which accrues from the instant amounts claimed since effective results are obtained using the compositions of Boyer.

With regards to instant claims 81 and 82, the granules of Boyer comprised of fenofibrate would be in non-reagglomerated form.

Given the explicit teachings of Boyer, the instant invention, when taken as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

* * * * *

Claims 16-55, 81 and 82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Curtet *et al.* (US Pat. No. 4,895,726).

Curtet *et al.* ('726) teach a fenofibrate composition comprising fenofibrate granules in combination with a solid surfactant, wherein the fenofibrate and solid surfactant have been co-micronized; a hydrosoluble carrier and a hydrophilic polymer, wherein the fenofibrate/solid

surfactant mixture granules have a mean particle size of less than 15 microns (see column 1, line 1 – col. 2, line 25); examples and claims.

Curtet *et al.* teach polyvinylpyrrolidone as the hydrophilic polymer employed. The hydrosoluble carrier taught is lactose (col. 2, lines 1-12). The preferred solid surfactant is sodium lauryl-sulfate in a recommended amount of between 0.5% and 7% (col. 1, lines 52-58). Excipients, such as magnesium stearate (lubricant) and starch (distintegrant) may also be added (col. 2, lines 1-4).

Curtet *et al.* teach a micronized fenofibrate composition containing a micronized mixture of particles of fenofibrate and a solid surfactant and method for preparing the fenofibrate composition comprising (i) intimately mixing and then co-micronizing the fenofibrate and the solid surfactant, (ii) adding lactose and starch to the mixture obtained, (iii) converting the whole to granules in the presence of water, (iv) drying the granules until they contain no more than 1% of water, (v) grading the granules, (vi) adding polyvinylpyrrolidone and magnesium stearate to the graded granules and (vii) filling gelatin capsules with the mixture obtained in stage (vi). The mean particle size of the micronized mixture obtained is less than 15 microns (μm) (column 2, lines 5-20).

Curtet *et al.* teach effective amounts of fenofibrate and a hydrophilic polymer-polyvinylpyrrolidone, wherein the fenofibrate is present in an amount of 200 mg per therapeutic unit (col. 1, lines 50-51) and the polyvinylpyrrolidone is contained in an amount of 7 mg (col. 3, lines 21-32).

While Curtet *et al.* do not explicitly teach the instantly claimed weight ratio of fenofibrate:hydrophilic polymer; surfactant:hydrophilic polymer, nor the instant amounts of

fenofibrate and carrier as claimed in claims 32-33 & 52-53, the Examiner points out that generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller,* 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). In this instance, Applicants have not demonstrated any superior or unexpected results, which accrue from the claimed weight ratios or amounts. The prior art vividly recognizes and teaches similar formulations comprising similar ingredients (fenofibrate, polymer, inert particles, etc.) that are used in the same field of endeavor to effectively treat the same problems (*i.e.*, hypercholesterolemia) as that desired by Applicants. No patentable distinction has been observed, which accrues from the instant amounts claimed since effective results are obtained using the compositions of Curtet *et al.*

Hence, given the explicit teachings of the art delineated above, the instant invention, when taken as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

* * * * *

Response to Arguments

Applicant's arguments filed 10/26/07 have been fully considered but they are not persuasive.

Rejection under 35 U.S.C. 103(a) over Boyer (US 4,800,079):

Applicant argued, "Applicants respectfully submit that Boyer does disclose or suggest the claimed fenofibrate to polymer ratio of between 1:10 and 4:1 as recited in independent claims 16 and 36. Boyer discloses a composition containing micronized fenofibrate, a polymer such as

polyvinylpyrrolidone (PVP), and possibly starch. The sole example that is provided in Boyerl comprises 400 kg of fenofibrate and 20 kg of PVP and/or methacrylate. As correctly pointed out by the U.S. Patent Office (PTO), Boyer's ratio of fenofibrate to polymer is 20:1. Boyer does not provide any motivation or suggestion to drastically reduce the weight ratio of fenofibrate to PVP of 20:1 to be any where near the claimed range of fenofibrate to polymer of between 1:10 and 4:1. The weight ratio in Boyer is significantly different than the claimed weight ratio and there is no motivation or suggestion to arrive at the claimed weight ratio of between 1:10 and 4:1. The ratio of fenofibrate to polymer in Boyer has more than 5 times fenofibrate to PVP than the claimed ratio of fenofibrate to polymer. One skilled in the art could not use routine experimentation to arrive at the claimed ratio because it would require one to drastically reduce Boyer's ratio to be 5 times less than stated to arrive at the claimed invention. Routine variation or experimentation would revolve around Boyer's ratio of 20:1, and not the claimed ratio that is 5 times smaller. In view of the significant difference in the ratios, the claimed ratio is not encompassed by Boyer and is not merely an optimization of the ratio described by Boyer. The Reginault Declaration provides a valuable comparison between Boyer and the claimed invention. The presently claimed invention has an unexpectedly superior dissolution profile when compared to Boyer."

Applicant's argument that "Boyer does not teach the claimed fenofibrate to polymer ratio of between 1:10 and 4:1", and that "as pointed out by the Office, Boyer teaches 400 kg of fenofibrate and 20 kg of PVP" was not persuasive, since Applicants have not sufficiently demonstrated any unexpected results, which accrue from the instant weight ratio, that results in a patentable disinction over the composition of Boyer. Admittedly, while Boyer uses high drug:polymer ratios, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical (*In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235(CCPA 1955)). In this instance, no criticality has been observed in the instant ratios over the ratios suggested by the prior art.

Regarding Applicant's argument that "Boyer uses a very specific process, which involves evaporation of the alcoholic solvent" was not persuasive. Applicant's arguments do not establish the scope of claims being presented. The instant claims are directed to composition claims. Thus, Applicant's argument relating to the use of alcohol solvent by Boyer does not negate the teachings of Boyer over the instant product limitations. Applicant's argument that "a disintegrating agent is absent from Boyer" was not persuasive since Boyer teaches use of a disintegrant, such as starch. See claims 3 & 7. Applicant's arguments relating to the superior dissolution profile as evidenced by the instant Declaration was not persuasive, because dissolution profiles are not being claimed herein. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In any event, Boyer meets the requirements of incorporating micronized fenofibrate, hydrophilic polymer and disintegrant components, the only deficiency being the claimed weight ratios, which as noted above, is a routinely optimized parameter that is attainable within the art.

Rejection under 35 U.S.C. 103(a) over Curtet (US 4,895,726):

Applicant argued, "Applicants respectfully submit that Curtet does disclose or suggest the claimed fenofibrate to polymer ratio of between 1:10 and 4:1 as recited in independent claims 16 and 36, nor the presence of a disintegrant. The claimed invention uses both a hydrophilic polymer and a disintegrating agent. Curtet fails to disclose the presence of both a hydrophilic polymer and a disintegrating agent because Curtet uses only a cross-linked polyvinylpyrrolidone (PVP). Curtet provides working examples comprising 200 grams fenofibrate and 7 grams cross-linked polyvinylpyrrolidone, such that the weight ratio of fenofibrate to cross-linked polyvinylpyrrolidone is 29:1. Curtet does not provide any motivation or suggestion to drastically

reduce the weight ratio of fenofibrate to polyvinylpyrrolidone (PVP) of 29:1 to the claimed range of fenofibrate to polymer of between 1:10 and 4:1. The weight ratio in Curtet is significantly different than the claimed weight ratio and there is no motivation or suggestion in any of the references to arrive at the claimed weight ratio of between 1:10 and 4:1. The ratio of fenofibrate to polymer in Curtet has greater than 7 times more fenofibrate to PVP than the claimed ratio of fenofibrate to polymer. There is simply no motivation in Curtet to drastically reduce the ratio used in Curtet to arrive at the claimed invention."

Applicant's argument that "Curtet does not suggest the claimed fenofibrate to polymer ratio of between 1:10 and 4:1" was not persuasive, since as noted above, no unexpected results have been demonstrated using the instant drug:polymer ratio. Applicant argues that "Curtet do not teach the presence of both a hydrophilic polymer and a disintegrant" was not persuasive. Note for instance, column 3, Table 1, lines 20-32, whereby Curtet discloses a fenofibrate preparation comprising both a hydrophilic polymer (polyvinylpyrrolidone) and disintegrant (starch). Thus, this argument was not persuasive. With regards to the Blouquin Declaration, the Declaration was not found persuasive. The Declaration presents dissolution profiles, which are not being claimed in the instant application.

* * * * *

Conclusion

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114.

See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

--No claims are allowed at this time.

* * * * *

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday-Friday during regular business hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley, can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Humera N. Sheikh/

Primary Examiner, Art Unit 1618

hns

September 26, 2008